In the Office Action, all pending claims, 4-12, were rejected under 35 U.S.C. § 112 first paragraph and 35 U.S.C. § 101. Applicants respectfully traverse these rejections.

Rejections Under 112, First Paragraph

The Examiner has rejected claims 4-12 under 35 U.S.C. § 112 first paragraph as containing subject matter not enabled by the specification. Applicants respectfully traverse this rejection.

According to the MPEP, the test of enablement is "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without any undue experimentation." MPEP § 2164.01 (citing *United States v. Telectronics, Inc.*, 857 F2d 778, 785 Fed. Cir. 1988). The MPEP also indicates that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. MPEP § 2165.04. As discussed below, the Examiner has cited the *Wands* factors but has failed to provide objective evidence that the claims are not enabled. To the contrary, analysis of the *Wands* factors demonstrates that the specification in fact meets the standard of enablement for the full scope of the claims.

The quantity of experimentation necessary

The Examiner has stated, without any factual support or objective evidence, that the quantity of experimentation is "on the order of several man-years," with little reasonable expectation of success. However, the MPEP at § 2164.01 states that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. MPEP § 2164.01, *citing In re Certain Limited Charge Cell Culture Microcarriers,* 221 U.S.P.Q. 1165, 1174 (International Trade Commission 1983).

The EGT assay can be performed by a single individual skilled in the art of molecular biology with minimal experience and where several hundred assays can be performed in a single day. Because it is expected that a haploid genome of 1 Mb contains at least 150 to 200 essential genes, one would expect identification of essential genes and/or sequences of interest in a reasonable time frame.

Further, each individual step in the method of claim 4, for example, such as mutagenizing by insertion of sequence tags, transforming host cells, growing host cells according to a variety

of selective conditions, amplifying DNA, and performing gel electrophoresis to resolve DNA fragments are standard techniques in the art.

For these reasons, the quantity of experimentation does not require several man-years, and in fact can be carried out by one skilled in the art using known, reproducible and reliable techniques.

The Amount of Direction or Guidance Provided

The Examiner states that the guidance provided by the specification is limited to specific genes of a single species. Applicants respectfully disagree. The specification contains a detailed discussion of the techniques utilized in the claimed method. Although the methodology of the EGT assay was tested solely with *Pseudomonas aeruginosa* as a prototype haploid organism, the technique has much broader applications and can be applied to all prokaryotes. The assay can be adapted to any viral, bacterial, fungal or eukaryotic cell that has a haploid genome and known sequences available in databases for primer synthesis.

The figures of the application show schematic representations of the technique, a physical and genetic map of an example of a suitable vector construct for use in the method of the invention, and results of the method carried out by the inventors. The specification also provides a detailed discussion of mutagenesis techniques (at least pp. 17-18 and 21-22), selective conditions (pp. 18-19), suitable insertional elements (p. 22), amplification methods (pp.24-25) and methods of detection of amplified products (p.23).

The Examples on pages 26-29 illustrate in detail the use of the disclosed method with *Pseudomonas aeruginosa* genes, including eight known genes which were tested to verify the method.

The Examiner represents that the disclosure fails to provide guidance for any type of cell. To the contrary, in addition to prokaryotes, at least pages 20-21 of the specification explain that the method of the invention will function for any haploid cell, including gametes, and is fully adaptable for organisms in which conversion to homozygosity is efficient and or complete. Because insertional mutagenesis of an essential gene, within the context of the invention, will result in the death of the cell, the genome of this cell will not be available as a substrate for the amplification process of the EGT method. As those of skill in the art are well aware, inactivation of an essential gene of any cell will result in the death of that cell, regardless of whether it is eukaryotic or prokaryotic.

The Presence or Absence of Working Examples

The Examiner's discussion of the working examples of the specification indicate that the Examiner has failed to appreciate the invention. The Examiner's discussion of Example 1 concludes that "the selective condition did not select for one group of cells over that of another." The methodology of the EGT assay does not rely on a selection of a group of cells over any other group of cells. The conditions that were tested in the specific case of *P. aeruginosa,* using bacterial cell division cell wall biosynthesis genes, does not rely on Kanamycin. It is well known in bacterial genetics and biochemical studies that these genes are essential regardless of the growth conditions. Therefore, the use of these genes in the Examples is particularly instructive because it demonstrates that the assay can identify true essential genes as well as genes that are essential only under special conditions.

According to MPEP § 2164.04 the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention (*citing In re Wright,* 999 F2d 1557, 1562 (Fed. Cir. 1993)). Section 2164.06(b) of the MPEP discusses *In re Wands*, 858 F2d 731 Fed. Cir. 1988, where the court concluded that undue experimentation would not be required to practice an invention relating to monoclonal antibody technology. This technology is in the same general field as the present invention. Similar to the case in *Wands*, the specification herein provides considerable direction in guidance in how to practice the claimed invention and also presents working examples. All of the methods that are needed to practice the invention are also known in the art, and the level of skill in the art is high. In *Wands* the applicant carried out the procedure for making a monoclonal antibody against hepatitis B surface antigen three times and was successful each time in producing at least one antibody which fell within the scope of the claims. Here, Applicant has utilized *P. aeruginosa* to successfully demonstrate that the invention application functions as intended and is therefore a useful tool in researching which genes of a given genome are essential.

The Nature of the Invention

The claimed invention relates to biotechnology. Although the Federal Circuit has recognized that this field is unpredictable, this factor alone does not preclude a finding of enablement. As the Federal Circuit has instructed, each factor in the enablement analysis must be considered and it is improper to conclude a disclosure is non-enabling based on only one of the factors, while ignoring others. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The State of the Prior Art

The Examiner states that the "prior art has developed to the point where it recognized that predicting properties and utilities of expressed modified proteins is quite unpredictable." The Examiner also states that the claimed method has "utility in the properties of the expressed proteins."

Applicants again respectfully assert that the Examiner has failed to appreciate the nature of the invention. The Application has nothing whatsoever to do with predicting properties of modified proteins. Rather, the invention is directed to the determination of whether an open reading frame, gene, or nucleotide sequence codes for an essential or dispensable protein or product.

The Specification, on page 21, notes that minimum stretches of sequence data must be available to design primers. The Examiner will agree that the art has developed to the point where sequencing polynucleotides is commonplace. In fact, as discussed, all of the individual techniques required to carry out the method of the invention are commonly performed in laboratories on a day-to-day basis, with predictable results. These include various insertional mutagenesis techniques, transformation of host cells, providing growth conditions for the cells, isolation and amplification of DNA, for example with PCR, and carrying out gel electrophoresis to resolve and visualize the DNA fragments.

The Relative Skill of Those in the Art

The Examiner recognizes that the skill of those in the art is high. Skilled artisans, armed with the teachings of the disclosure and the techniques that have been developed in the field of biotechnology, would have little difficulty in using the identification techniques presented in the Application.

The Breadth of Scope of the Claims

As discussed, Applicants respectfully assert that the EGT assay can be adapted to any viral, bacterial, fungal or eukaryotic cell that has a haploid genome and known sequences available in databases for prior synthesis and screening by PCR and/or other methods for nucleic acid amplification. For example, at least at page 24, the specification discusses the application of

the assay to potato blight virus, equine encephalitis virus, cytomegalovirus, and eukaryotic disease-causing organisms. The Examiner has not provided objective evidence to the contrary.

Conclusion

Based upon the foregoing analysis, it is believed that the pending claims fully comply with 35 U.S.C. § 112, first paragraph. Notification to that effect is earnestly solicited.

Rejections under 35 U.S.C. § 101

The MPEP at § 2107.02 states that any rejection based on lack of utility should include a detailed explanation why the claimed invention has no specific and substantial credible utility. The same section also states that the *prima facie* showing must contain the following elements: (a) an explanation that clearly sets forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; (b) support for factual findings relied upon in reaching this conclusion; and (c) an evaluation of all relevant evidence of record including utilities taught in the closest prior art. The section also states that when the Examiner is specific, the Applicant is then able to identify the assumptions made by the Office in setting forth the rejection and will be able to address those assumptions properly.

Here, the Examiner has been far from specific. The Examiner has not fully comprehended the invention, the uses of which are amply discussed in the specification, and which are readily understood by those of skill in the art. For example, the specification at page 4 discusses that by allowing the user to identify essential genes in an organism, the EGT assay permits the ready identification of therapeutic targets. At page 2, the potential and ramifications of the ability to identify essential genes is discussed. Important uses of the assay include not only the identification of targets for therapy in antimicrobial research, but also the ability to yield important information about higher organisms relating to, for example, cellular homeostasis and cancer. The invention of the application provides a simple and efficient method of identifying essential genes either under specific conditions or non-selective conditions, adaptable according to the interests of the investigator.

As the Applicants have asserted specific, credible utility, and have enabled the claims by the present specification, it is strongly urged that the pending objection based upon lack of asserted utility be withdrawn.

CONCLUSION

In view of the remarks presented herein, it is respectfully submitted that the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact the Applicant's undersigned representative if Examiner believes that doing so will expedite the prosecution of the application.

Respectfully submitted,

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